BIOTECH'S MOST RESPECTED NEWS SOURCE FOR MORE THAN 20 YEARS

BIOWORLD® TODAY

THE DAILY BIOPHARMACEUTICAL NEWS SOURCE

THURSDAY
MARCH 15, 2012

VOLUME 23, NO. 51

Smarticles Extend Their Reach In ProNAi's DNAi Approach

By Marie Powers
Staff Writer

ProNAi Therapeutics Inc. became the second biotech to validate a savvy technology purchase by Marina Biotech Inc., extending its license for Marina's "Smarticles" liposomal delivery technology – used in its nucleic acid-based DNA interference (DNAi) therapies – from the clinic to potential commercialization.

Under the terms of an exclusive licensing agreement, Marina, of Bothell, Wash., could receive up to $14 million in up-front, clinical and commercialization milestone payments plus sales royalties for each gene target selected by privately held ProNAi, which is responsible for developing and commercializing resulting products. The open-ended agreement gives ProNAi the option to select any number of gene targets, potentially catapulting the deal's value into tens or even hundreds of millions of dollars for Marina.

See Marina, Page 3

Holy Grail of HCV Vaccine May Be Within Okairos' Reach

By Mari Serebrov
Washington Editor

While other drugmakers are spending billions of dollars in pursuit of the next-generation hepatitis C treatment, Okairos AG is on a quest for the holy grail – a preventive hepatitis C virus (HCV) vaccine.

In the wake of promising Phase I immunogenicity data, the Basel, Switzerland-based biotech has initiated a proof-of-concept Phase I/II trial of its ProCvax vaccine, which is designed to stimulate a strong T-cell response to HCV.

Part of a collaboration with the National Institute of Allergy and Infectious Diseases, the trial is the first randomized, placebo-controlled study of a vaccine to prevent HCV infection. The endpoints are safety and incidence of chronic HCV infection.

If successful, ProCvax could do in the HCV space

See Okairos, Page 4

Financings Roundup

Kala Tops Off Seed Round with Additional $6.2M Equity Deal

By Catherine Shaffer
Staff Writer

Kala Pharmaceuticals Inc., of Waltham, Mass., raised $6.2 million in equity financing from its existing investors. The new round completes its seed financing of $11.2 million to support its pipeline in diseases affecting mucosal tissues, including cystic fibrosis.

The company also is receiving funding from the National Heart, Lung, and Blood Institute for an inhaled treatment for cystic fibrosis-related infection, and from the National Eye Institute for new formulations of ocular drugs.

Kevin Pojasik, vice president of corporate development for Kala, said the funding would last through 2012 and the first quarter of 2013.

"There's a nice opportunity for a partnership or two with a major company that could help drive us forward," he said.

See Financings Roundup, Page 5

NewCo News

Gradalis Emerges from Stealth With Phase II Cancer Vaccine

By Trista Morrison
Staff Writer

Cancer vaccines, long the red-headed stepchildren of biotech, were briefly catapulted into the limelight by Dendreon Corp.'s 2010 approval of Provenge (sipuleucel-T) only to be dragged back down by that drug's disappointing sales.

Gradalis Inc. has no intention of following in Dendreon's footsteps – at least not commercially. The Dallas-based start-up's Phase II personalized cancer vaccine differs from Provenge on both scientific and business fronts, according to its president, CEO and co-founder, David Shanahan.

FANG, which stands for Furin-ANd-GMCSF, is created

See Gradalis, Page 6

AHC Media

Marina

Continued from page 1

Investors noticed the deal. On Wednesday, Marina's shares (OTCQX:MRNA) gained 18 percent, or 9 cents, closing at 59 cents.

Ann Arbor, Mich.-based ProNAi is a venture-backed biotech developing a class of drugs that use single strands of unmodified DNA oligonucleotides to target genomes responsible for complex, proliferative diseases – initially in cancer. The company's lead drug candidate, PNT2258, demonstrated safety and in vivo efficacy in a variety of preclinical tumor xenograft models.

ProNAi originally licensed the Smarticles delivery technology in 2007 from Novosom AG, of Halle, Germany, for diseases targeted by its lead compound in exchange for undisclosed up-front, milestone and royalty payments composed of a mixture of cash and equity. At the time, ProNAi retained an option on four additional DNAi targets.

The Smarticles technology comprises charge-reversible, amphoteric liposome carriers that switch from having a negative charge in the bloodstream to having a positive charge as they undergo endocytosis by macrophages, enabling them to deliver their payload efficiently. The specificity of individual Smarticles formulations can be tuned by varying their lipid composition.

In July 2010, Marina acquired Novosom's Smarticles intellectual property for $5 million in unregistered Marina common stock.

At the time, the acquisition went almost unnoticed. Marina is developing oligonucleotide-based therapeutics using multiple mechanisms of action, including RNA interference (RNAi) and messenger RNA translational blocking. Its pipeline includes a clinical program in familial adenomatous polyposis – a precancerous syndrome – and preclinical programs in bladder cancer and malignant ascites.

Last year, the company inked a $25 million agreement with the Debiopharm Group, of Lausanne, Switzerland, to develop and commercialize the bladder cancer program.

Marina didn't necessarily see an immediate application for the Smarticles technology in its own pipeline, but "we saw great opportunity in the Smarticles delivery technology for a variety of nucleic acid-based approaches," J. Michael French, Marina's president and CEO, told *BioWorld Today*. "ProNAi represents just one approach."

ProNAi currently is running a Phase I dose-escalation study of PNT2258 in advanced solid tumors. That study is evaluating safety and tolerability, maximum tolerated dose, pharmacokinetics and pharmacodynamics of the compound, a DNAi oligonucleotide targeted against the anti-apoptotic Bcl-2 oncogene.

The Smarticles delivery technology, which contains no chemical modifications, offers protection for the DNAi oligonucleotide during systemic administration, enabling good circulation times and extrahepatic tumor exposure, explained Wendi V. Rodrigueza, ProNAi's vice president of product development.

To its knowledge, ProNAi is the only biotech applying DNAi – short single-strand unmodified oligonucleotides designed to silence genes by interfering with DNA – to cancer therapeutics, added Mina Sooch, a general partner at Apjohn Ventures and a member of ProNAi's board. In contrast to RNAi, antisense or miRNA, the DNAi silencing approach targets genomic sequences within the noncoding region of DNA, disrupting transcription.

"The elegant simplicity of the single strand" is a key differentiator in ProNAi's approach, Sooch said.

Early Phase I data suggested the trial will validate the company's preclinical studies of PNT2258, according to Sooch. ProNAi plans to report Phase I results later this year and to initiate Phase I/II safety and efficacy studies as quickly as possible following its Phase I analysis.

The company, which has raised more than $20 million from venture funds, angels and grants from the state of Michigan, expects to close a $15 million Series C in the near future, Sooch said. The financing would give the company a runway of at least two years and enable it to fund the Phase I/II studies.

Ultimately, ProNAi would seek to partner the program with a large biotech or pharma following Phase II studies.

Knowledge gained from clinical studies of PNT2258 could enable the company to advance additional drug candidates targeting other oncogenes, including c-Myc and KRAS, while exploring additional disease targets in areas such as inflammation and genetics diseases, she added.

Each new target means additional revenue for Marina, which has begun to use the Smarticles in its internal research programs and has an additional collaboration with Mirna Therapeutics Inc., of Austin, Texas.

That deal, inked in December 2011 for $63 million in up-front and milestone payments plus royalties on product sales, covers the application of Smarticles technology to Mirna's pipeline of microRNA tumor suppressors, which also are in clinical testing. (See *BioWorld Today*, Dec. 28, 2011.)

The ProNAi license broadens the application of Smarticles technology to the systemic administration of both single- and double-stranded oligonucleotide therapeutics, French observed.

"We clearly saw the role of Smarticles in the broader nucleic acid space," he said.

By using Smarticles and its DiLA2 delivery technology – a mechanism for creating liposome formulations from dialkylated amino acids to deliver UsiRNA – "we're looking at not only how we can advance our internal programs but, more importantly, how we can establish partnerships with pharma," French added. ■